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D9903023.071101

1. A method for diagnosing a malignant neoplasm in a mammal, comprising contacting a bodily fluid from said mammal with an antibody which binds to an human aspartyl (asparaginyl) beta-hydroxylase (HAAH) polypeptide under conditions sufficient to form an antigen-antibody complex and detecting the antigen-antibody complex.

2. The method of claim 1, wherein said neoplasm is derived from endodermal tissue.

- 3. The method of claim 1, wherein said neoplasm is selected from the group consisting of colon cancer, breast cancer, pancreatic cancer, liver cancer, and cancer of the bile ducts.
- 4. The method of claim 1, wherein said neoplasm is a cancer of the central nervous system (CNS).
- 5. The method of claim 1, wherein said bodily fluid is selected from the group consisting of a CNS-derived bodily fluid, blood, serum, urine, saliva, sputum, lung effusion, and ascites fluid.
- 6. The method of claim 1, wherein said antibody is a monoclonal antibody.
- 7. The method of claim 6, wherein said monoclonal antibody is FB50.
- 8. The method of claim 6, wherein said monoclonal antibody is selected from the group consisting of 5C7, 5E9, 3 19B, 48A, 74A, 78A, 86A.

A method for prognosis of a malignant neoplasm of a mammal, comprising (a) contadting a bodily fluid from said mammal 3 with an antibody which binds to an HAAH polypeptide under 4 conditions sufficient to form an antigen-antibody complex 5 and detecting the artigen-antibody complex; 6 (b) quantitating the amount of complex to 7 determine the level of HAAH in said fluid; and 8 9 (c) comparing the level of HAAH in said fluid 10 with a normal control level of HAAH, wherein increasing levels of HAAH over time indicates an adverse prognosis. 11 10. A method of inhibiting tymor growth in a mammal 1 comprising administering to said makmmal a compound which inhibits expression of HAAH. 11. The method of claim 1/0, wherein said compound is a HAAH antisense nucleic acid. IJ 12. The method of claim 1/0, wherein said compound 2 is a ribozyme. The method of claim 10, wherein said tumor is 2 derived from endodermal tissue. The method/of claim 10, wherein said tumor is 1 2 selected from the group consisting of colon cancer, breast 3 cancer, pancreatic carcer, liver cancer, and cancer of the

The method of claim 10, wherein said tumor is a

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bile ducts.

CNS tumor.

1	16. A method of inhibiting tumor growth in a mammal
2	comprising administering to said mammal a compound which
3	inhibits an enzymatic activity of HAAH.
1	17. The method of claim 16, wherein said enzymatic
2	activity is hydroxylase activity.
1	18. The method of claim 16, wherein said compound
2	is a dominant negative mutant of HAAH.
1	19. The method of claim 18, wherein said dominant
2	negative mutant HAAH comprises a mutation in a catalytic
3	domain of HAAH.
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<u>ā</u> 1	20. The method of claim 16, wherein said compound
<mark>무</mark> 2	is an HAAH-specific intrabody.
Ü	$\mathcal{L}_{\mathcal{A}}$
	21. The method of claim 16, wherein said compound
2	is L-mimosine.
1	22. The method of claim 16, wherein said compound
<u></u> 같	is a hydroxypyridone.
i.i i.i.	
1	23. A method of inhibiting tumor growth in a mammal
2	comprising administering to said mammal a compound which
3	inhibits signal transdyction through the IRS signal
4	transduction pathway.
1	24. The method of claim 23, wherein said compound
2	inhibits IRS phosphorylation.
1	25. The method of claim 23, wherein said compound
2	inhibits binding of Fos or Jun to an HAAH promoter sequence.

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that binds to an epitope of HAAH linked to a cytotoxic

cells compared to non-tumor cells.

comprising the antibody of claim 29.

agent, wherein said composition preferentially kills tumor

34. A kit fof diagnosis of a tumor in a mammal,

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A method of inhibiting tumor growth in a mammal

comprising administering to said mammal a compound which

inhibits HAAH hydroxylation of a NOT H polypeptide.

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- 1 35. The kit of claim 34, wherein said antibody is immobilized on a solid phase. 2
- 1 The kit of claim 35, wherein said solid phase is selected from a group consisting bf an assay plate, an 2 assay well, a nitrocellulose membrahe, a bead, a dipstick, 3 4 and a component of an elution column.
  - A method of determining whether a candidate compound inhibits HAAH enzymatic activity, comprising
    - (a) providing a HAAH polypeptide;
  - (b) providing a polypeptide comprising an EGF-like domain;
  - (c) contacting said HAAH polypeptide or said NOTCH polypeptide with said candidate compound;
  - (d) determining hydroxylation of said polypeptide of step (b), wherein a decrease in hydroxylation in the presence of said candidate compound compared to that in the absence of said compound indicates that said compound inhibits HAAH enzymatic activity.
  - 38. A method of determining whether a candidate compound inhibits HAAH /activation of NOTCH, comprising
    - (a) providing a cell expressing HAAH;
    - (b) contacting said cell with a candidate compound;

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> (c) measuring translocation of activated NOTCH to the nucleus of said/cell, wherein a decrease in translocation in the presence of said compound compared to that in the absence of said compound indicates that said compound HAAH activation of NOTCH.